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Inside this supplement: Antimicrobial resistance

Antimicrobial resistance (AMR) is an emerging global public health issue that could affect any one of us. Most antibiotic use in Canada is not in humans—it is in livestock. Thus, addressing AMR involves not only our medical systems, but also veterinary medicine, the Canadian Food Inspection Agency, and Agriculture and Agri-Food Canada. Learn about how all the key federal partners have come together on a Federal Framework for Action, the extent of AMR in Canada, and how we are starting to be exposed to AMR organisms in the meat we eat, and then read about a national information campaign that will soon be launched to mark Antibiotic Awareness Week, November 17-21, 2014.

Upcoming webinars

November 17, 2014: Launch of the Public Health Agency of Canada AMR Awareness Campaign
https://gts-ee.webex.com/gts-ee/onstage/g.php?d=553761831&t=a

November 20, 2014: Antimicrobial Use and Resistance in Canada—Surveillance Update
https://gts-ee.webex.com/gts-ee/onstage/g.php?d=556860062&t=a

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Canada

Antimicrobial resistance and use in Canada: A federal framework for action

Public Health Agency of Canada,* in participation with the Canadian Food Inspection Agency, Canadian Institutes of Health Research, Health Canada, and Agriculture and Agri-Food Canada

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Abstract

Antimicrobial resistance (AMR) is a serious and growing global public health threat. Modern medical and veterinary practice depends on the widespread availability of effective antimicrobials to prevent and treat infections in humans and animals. Addressing the growing threat of AMR in Canada is a shared responsibility; *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* serves as a starting point for a collaborative response. The goal of the Framework is: "To protect Canadians from the health risks related to antimicrobial resistance." It includes three pillars: Surveillance, Stewardship, and Innovation. The Framework identifies concrete Government of Canada actions to reduce the threat and impact of AMR. Equally important, it is a vehicle to engage partners and stakeholders in discussions on efforts that, together, can significantly increase the results of individual actions. Beyond the Government of Canada, provinces and territories, academia, animal and human health professionals, food production stakeholders, animal producer groups and farmers, as well as private industry each hold essential levers to reduce AMR. By continuing to work together, we will collectively achieve greater results in reducing the risks of antimicrobial resistance and protecting the health and safety of all Canadians.

Introduction

Antimicrobial resistance (AMR) is a serious and growing global public health threat. Governments and health organizations around the world are paying increasing attention to the significant threat that this problem poses to modern medicine and the health of the global population. *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* is a just released publication that represents the Government of Canada's response to the threat of AMR (1). It provides a cohesive and collaborative approach across federal departments with mandates to address and mitigate AMR. Within Canada, this Framework will serve as a starting point for engagement and mobilization of all who are accountable for action on antimicrobial resistance and use.

Why is antimicrobial resistance a problem?

Modern medical and veterinary practice depends on the widespread availability of effective antimicrobials to prevent and treat infections in both humans and animals. Without them, the ability to fight infectious disease is significantly impeded. Each year in Canada, more than 18,000 hospitalized patients acquire infections that are resistant to antimicrobials. Deaths directly related to *Clostridium difficile* alone have increased five-fold in the past decade (2, 3).

Why are we taking action now?

There are activities that can be undertaken and expanded upon that will protect Canadians from the threat of AMR. However, with the increasing burden of antimicrobial resistance, the time to act is now. Domestic action is mirrored by a global call for action; World Health Assembly Member States endorsed a resolution that identified "the urgent need of a Global Action Plan for antimicrobial resistance" (4). Canada's Framework for Action represents an important step in expanding domestic efforts and responding to the global call for action on antimicrobial resistance.

A shared responsibility

Addressing the growing threat of AMR in Canada is a shared responsibility. The Government of Canada's role in protecting Canadians against disease threats of national concern is essential to multi-sector collaboration. The federal role for AMR is included in the mandate of several departments: Public Health Agency of Canada (PHAC), Health Canada (HC), Canadian Food Inspection Agency (CFIA), Canadian Institutes of Health Research (CIHR), and Agriculture and Agri-food Canada (AAFC). Provinces and territories play a key role because they are responsible for the delivery of health care, approval of antimicrobials for medical coverage, and the regulation of antimicrobial use in agriculture and veterinary medicine. Professional and non-governmental organizations are also actively involved in addressing antimicrobial resistance and use.

The Framework

The goal of the Framework for Action is: "To protect Canadians from the health risks related to antimicrobial resistance." The federal government will take action and work with its partners to reduce the health risks associated with AMR in three areas: Surveillance, Stewardship, and Innovation.

Surveillance

Surveillance systems collect data and information that is used to protect the health of human and animal populations. Antimicrobial surveillance information informs effective antimicrobial resistance and antimicrobial use programs, guidelines, and policies.

ACTION 1: ***Establish and strengthen surveillance systems to identify new threats or changing patterns in antimicrobial resistance and use, in human and animal settings.***

Canada has well-established surveillance systems for antimicrobial resistance and use. The Canadian Antimicrobial Resistance Surveillance System (CARSS) will be created, building on the foundation of the Public Health Agency of Canada's current antimicrobial resistance surveillance systems. CARSS will integrate available antimicrobial resistance data, clearly articulate and track antimicrobial resistance at a national level, and expand surveillance activities at the hospital and community level.

CFIA, AAFC, HC, and PHAC collaborate on the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). Moving forward this work will be strengthened and linked to CARSS. For example, CFIA and AAFC are planning increased surveillance on antimicrobial use in animal settings to ensure that a comprehensive data set is available through CIPARS.

These and other actions will provide a broader understanding of antimicrobial use and resistance across human populations in hospital and in the community, and animals in veterinary and agricultural settings—all in support of keeping antimicrobials effective.

Stewardship

Conserving the effectiveness of currently available antimicrobials is vital in mitigating the threat posed by antimicrobial resistant microbes. Public awareness activities help Canadians understand the benefits and risks of antimicrobials. The public plays a key role in infection prevention through day-to-day practices such as good hand hygiene.

ACTION 2: ***Strengthen the promotion of the appropriate use of antimicrobials in human and veterinary medicine.***

The Government of Canada will engage the public through an Antimicrobial Resistance Awareness Campaign on antimicrobial use and infection control during Antibiotic Awareness Week 2014 (November 17–21). Future awareness activities will build on lessons learned from these activities. Health Canada is working to increase veterinary oversight of the use of medically important antimicrobials in food animal production. Efforts are also currently underway to phase out growth promotion claims on medically important antimicrobials.

ACTION 3: ***Work with the animal agriculture sector partners to strengthen the regulatory framework on veterinary medicines and medicated feeds, including facilitating access to alternatives, and encourage the adoption of practices in order to reduce the use of antimicrobials.***

The Government of Canada's role in the regulation of animal health includes the sale of veterinary drugs, medicated feeds, and vaccines. Its regulatory activities present an opportunity to further advance stewardship and the adoption of best practices in Canada. Through legislative and regulatory authorities, the Government can engage with those who must comply with the regulations to identify innovative approaches to facilitate access to alternatives.

Innovation

Innovation fosters new methods and tools that combat AMR and improve antimicrobial use. Research informs health services and policy through innovative solutions, ranging from new or alternative antimicrobials and therapies, through faster and more accurate diagnostics. The federal government supports ongoing domestic health research and innovation while collaborating with international partners to contribute to global research efforts on antimicrobial resistance, antimicrobial use, novel therapies, and alternative antimicrobials.

ACTION 4: ***Promote innovation through funding collaborative research and development efforts on antimicrobial resistance both domestically and internationally.***

The Government of Canada is committed to increasing its research investment to support innovation. Through the CIHR-funded Canada–U.K. partnership on antimicrobial resistance, and other CIHR-funded research projects, research is currently underway to better understand the nature of resistance, investigate novel therapies, identify alternatives to antimicrobials, develop diagnostic tools, and find new ways of using existing antimicrobials.

Moving forward

The Framework identifies concrete Government of Canada actions to reduce the threat and impact of antimicrobial resistance. Equally important, it is a vehicle to engage partners and stakeholders in discussions on efforts that, together, can significantly increase the results of individual actions. Beyond the Government of Canada, provinces and territories, academia, animal and human health professionals, food production stakeholders, animal producer groups and farmers, as well as private industry each hold essential levers to reduce antimicrobial resistance. Working in collaboration will support efforts across both human and animal health settings.

Conclusion

Canada is already taking significant action to address the threat of AMR both domestically and internationally. By continuing to work together, we will collectively achieve greater results in reducing the risks of antimicrobial resistance and protecting the health and safety of all Canadians.

Acknowledgements

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Conflict of interest

None.

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Antimicrobial resistance surveillance in Canadian hospitals, 2007–2012

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Abstract

Background: The Canadian Nosocomial Infection Surveillance Program (CNISP) is a collaborative effort of the Public Health Agency of Canada's Centre for Communicable Diseases and Infection Control, the National Microbiology Laboratory, and 54 largely university-affiliated tertiary care sentinel hospitals in 10 provinces across Canada.

Objective: To provide a summary of antibiotic resistance rates of four key antibiotic resistant organisms in major hospitals across Canada from January 1, 2007, to December 31, 2012.

Methods: Patients' clinical and demographic data and associated results of laboratory analyses were submitted to the Agency by participating hospitals. The infection rates were summarized per 1,000 patient admissions at national and regional levels.

Results: In Canada, the overall health care-associated *Clostridium difficile* infection (HA-CDI), HA-CDI rates peaked in 2008 at 5.8 HA-CDI infections per 1,000 patient admissions then remained stable between 2009 and 2012 at approximately 5 HA-CDI infections per 1,000 admissions; the West and Central regions had higher rates than the Eastern region. The rates of methicillin-resistant *Staphylococcus aureus* (MRSA) peaked in 2009 at 9.5 MRSA infections per 1,000 patient admissions then decreased to 8.8 MRSA infections per 1,000 admissions in 2012, with the Central region having higher rates than the Western and Eastern regions. The rates of vancomycin-resistant *Enterococci* (VRE), have been low but rising with 0.08 VRE infections per 1,000 patient admissions in 2007, gradually rising to 0.5 VRE infections per 1,000 admissions in 2012, with consistently higher rates in the Western region, slightly lower rates in the Central region and the lowest rates in the Eastern region. The rates of carbapenem-resistant *Enterobacteriaceae* (CRE) have been measured since 2010 and have been low and stable, with 0.11 CRE infections per 1,000 patient admissions in 2010 and 0.14 CRE infections per 1,000 admissions in 2012, with higher rates in the Western and Central regions and lower rates in the Eastern region.

Conclusion: In Canada, of the four antibiotic resistant organisms under surveillance, HA-CDI and MRSA have been gradually decreasing, VRE is low but rising, and CRE remains low with Western and Central rates consistently higher than Eastern rates.

Introduction

Since the initial use of antibiotics in the 1940s, resistant strains of bacteria have emerged. Increasingly however, antibiotic resistance is seen as a challenge in both clinical care and public health. Antibiotic resistance has spread around the world, affecting both human health and the food supply.
The Public Health Agency of Canada (the Agency or PHAC) collects national data on antimicrobial resistant organisms in humans through the Canadian Nosocomial Infection Surveillance Program (CNISP). This is a collaborative effort of the Centre for Communicable Diseases and Infection Control, the National Microbiology Laboratory (NML) and sentinel hospitals across Canada that participate as members of the Canadian Hospital Epidemiology Committee, a subcommittee of the Association of Medical Microbiology and Infectious Disease Canada (AMMI). CNISP is intended to identify trends and inform infection prevention and control programs and policies across the country.

The CNISP surveillance reports are published on a regular basis. The objective of this paper is to provide a summary of antibiotic resistance rates of four key antibiotic resistant organisms in major hospitals across Canada: health care-associated *Clostridium difficile* infection (HA-CDI), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and carbapenem-resistant *Enterobacteriaceae* (CRE). This paper focuses on trends for both adult and children hospitalized in participating CNISP hospitals based on patient admissions per year. The most recent full CNISP report, *Antimicrobial Resistant Organisms (ARO) Surveillance—Surveillance Report for Data from January 1 2007 to December 31 2012*, is available online (1).

Methods

Data collection

Case definitions were agreed upon for each of the four organisms. Following a case identification in one of the participating hospitals, a standardized patient questionnaire was completed that included patient demographics, clinical information, previous hospitalization within the past 12 months, and site of positive culture. Data were then submitted electronically through a web-based information management system, the Canadian Network for Public Health Intelligence (CNPHI), to PHAC for further statistical analysis and storage. Participating hospitals also provided the Agency with the number of patient-admissions and the number of patients-days for the corresponding surveillance year. [Note: very slight differences in reported numbers occur in this paper compared to the online report due to recent updates from participating sites; where differences exist, CCDR should be taken as correct.]

Standard National Healthcare Safety Network (NHSN) surveillance definitions that include both laboratory and clinical criteria were used to determine infection. (If there were no clinical signs, the patient was determined to be colonized; not infected.)

Laboratory analysis

Based on an agreed upon protocol for each organism, a sampling of isolates were sent to the National Microbiology Laboratory (NML) for molecular testing. The NML sent the laboratory results to PHAC through CNPHI as well. Both the laboratory results and data collected through the patient questionnaires were linked using a unique, anonymized patient identifier.

Data analysis

Data from both participating hospitals and the NML were extracted, validated, and statistically analyzed by PHAC staff. Infection rates per 1,000 patient admissions were calculated by dividing the number of cases over the total number of admissions per year multiplied by 1,000. Rates are calculated using only eligible data, that is to say only the hospitals that supplied both numerator (cases) and denominator

(patient admissions) data are used to calculate the rates. For reporting purposes, and to ensure confidentiality, provinces were grouped into three regions: Western (British Columbia, Alberta, Saskatchewan, and Manitoba), Central (Ontario and Québec), and Eastern (Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador). (Prince Edward Island began submitting data in 2011; the territories do not currently submit data.) Surveillance at participating hospitals is considered to be within the mandate of hospital infection prevention and control programs and does not constitute human research; therefore, no research ethics board approval was sought.

Results

Health care-associated *Clostridium difficile*

Clostridium difficile is the most common cause of infectious diarrhea and pseudomembranous colitis in hospitals and long-term care facilities in Canada (2). *C. difficile* causes a range of illness from no symptoms at all to a severe, life-threatening disease (3). The population at risk of acquiring *Clostridium difficile* infection (CDI) includes the elderly, or people with certain antibiotics exposure, immunocompromising conditions or serious underlying disease. Only health-care associated cases of *C. difficile* are reported here as per the case definition (see box below).

Case definition of hospital-acquired *Clostridium difficile* infection

A patient is identified as having *Clostridium difficile* infection (CDI) if the patient:

- has diarrhea or fever, abdominal pain and/or ileus, and a laboratory confirmation of a positive toxin assay or positive polymerase chain reaction (PCR) test for *C.difficile*;
- has a diagnosis of pseudomembranes on sigmoidoscopy or colonoscopy or histological/ pathological diagnosis of CDI; or
- is diagnosed with toxic megacolon (in adult patients only).

In addition, a patient is considered to have hospital-acquired *Clostridium difficile* infection (HA-CDI) if:

- the patient's CDI symptoms occur in the admitting hospital less than 72 hours after admission; or
- CDI is seen in a patient who had been hospitalized in the admitting hospital and discharged within the previous four weeks.

In Canada, national rates of health care-associated *Clostridium difficile* infection (HA-CDI) peaked in 2008 at 5.8 HA-CDI infections per 1,000 patient admissions then remained stable between 2009 and 2012 at approximately 5 HA-CDI infections per 1,000 admissions; the West and Central regions had higher rates than the Eastern region (**Figure 1**).

FIGURE 1. National and regional Health care-associated *Clostridium difficile* Infection (HA-CDI) incidence rates per 1,000 patient admissions, January 1, 2007 to December 31, 2012. N = 18,871

	2007	2008	2009	2010	2011	2012
West	4.1	6.4	4.9	4.6	4.6	4.8
Central	5.1	6.1	5.0	5.1	5.9	5.3
East	3.4	3.6	2.5	2.0	2.2	2.6
Overall	4.5	5.8	4.7	4.5	5.1	4.8

Overall, the North American pulsed field type 1 (NAP 1) strain was the most dominant strain. Of the 2,497 submitted stool specimens, the NAP 1 strain was found in 1,059 (42.4%) specimens; 11.0% were NAP 4 strain type and 10.3% were NAP 2 (data not shown).

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Staphylococcus aureus (*S. aureus*) typically colonizes the skin and mucosal surfaces of healthy humans. It can also cause wound, urine, skin and soft tissue infections, osteomyelitis, endocarditis, and bacteremia. *S. aureus* can be acquired in the community or in the hospital or other health care settings such as long-term care, dialysis, and rehabilitation facilities. *S. aureus* is particularly successful in becoming antibiotic resistant, explaining in part its high associated burden of disease worldwide (4). MRSA is a *S. aureus* that has become resistant to first line beta-lactam antibiotics such as methicillin, oxacillin, penicillin, and amoxicillin. Only health care-associated cases of *Clostridium difficile* are reported here as per the case definition (see box below).

Case definition of methicillin-resistant *Staphylococcus aureus* (MRSA) infection

- Isolation of *Staphylococcus aureus* from any body site

AND

- Resistance of isolate to oxacillin

AND

- Patient must be admitted to the hospital

AND

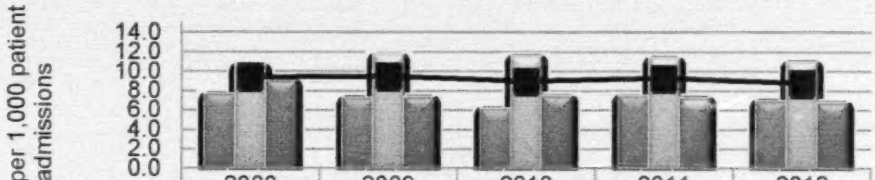
- Is a "newly identified MRSA case" at a participating CNISP hospital at the time of hospital admission or identified during hospitalization

This includes:

- MRSA cases identified for the first time during this hospital admission
- Cases that have been previously identified at other non-CNISP hospitals

The rates of MRSA peaked in 2009 at 9.5 MRSA infections per 1,000 patient admissions then decreased to 8.8 MRSA infections per 1,000 admissions in 2012. Rates in the Central region have increased slightly since 2008 and are higher than the national average in each surveillance year (**Figure 2**).

FIGURE 2. National and regional methicillin-resistant *Staphylococcus aureus* (MRSA) infection and colonization rates per 1,000 patient admissions, January 1, 2008 to December 31, 2012. N = 9,650



	2008	2009	2010	2011	2012
West	7.7	7.3	6.2	7.5	7.0
Central	10.7	11.8	11.6	11.4	11.0
East	9.1	7.4	7.5	7.3	6.8
Overall	9.4	9.5	9.0	9.3	8.8

Infections identified as skin, soft tissue or burn were the most common source of MRSA clinical infections and represent, on average, approximately 40% of all clinical infections over the surveillance period. From 2008 to 2012, approximately 9% of patients with a clinical MRSA infection died, and 25% of patients with a MRSA bloodstream infection died at 30 days after the date of positive culture.

Vancomycin-resistant *Enterococci* (VRE)

VRE infections occur most commonly among those who are hospitalized and immunocompromised, who have been previously treated with vancomycin or other antibiotics for long periods of time, or who are older and have undergone surgical procedures or who have indwelling medical devices such as urinary catheters (see box below).

Case definition of vancomycin-resistant *Enterococci*

Any inpatient from whom *Enterococcus faecium* or *Enterococcus faecalis* having a minimum inhibitory concentration of vancomycin of ≥8 ug/mL was isolated from a clinical specimen.

The rates of VRE have been low but rising with 0.08 VRE infections per 1,000 patient admissions in 2007, rising to 0.5 VRE infections per 1,000 admissions in 2012, with consistently higher rates in the Western region, slightly lower rates in the Central region, and the lowest rates in the Eastern region (**Figure 3**). The *vanA* gene remains the predominant gene among VRE bloodstream infections.

FIGURE 3. National and regional vancomycin-resistant *Enterococci* (VRE) infection incidence rates per 1,000 patient admissions, January 1, 2007 to December 31, 2011. N = 1,510

	2007	2008	2009	2010	2011	2012
West	0.11	0.32	0.4	0.6	0.7	0.6
Central	0.06	0.08	0.2	0.2	0.5	0.4
East	0.01	0.00	0.02	0.00	0.03	0.03
Overall	0.08	0.16	0.2	0.3	0.5	0.5

Carbapenem-resistant *Enterobacteriaceae* (CRE)

Gram-negative bacilli cause a variety of diseases, ranging from pneumonia to urinary tract infections, wound infections to septicemia. They typically occur in ill patients with exposure to acute and long-term care settings. Infections are commonly caused by species belonging to the *Enterobacteriaceae* family, such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloaca*. These bacteria are often resistant to many commonly prescribed antibiotics, but typically remain susceptible to the carbapenem group of antimicrobials. There are currently no new antibiotics in development to combat bacteria resistant to carbapenems. The case definition of carbapenem-resistant *Enterobacteriaceae* has evolved over time (see box below).

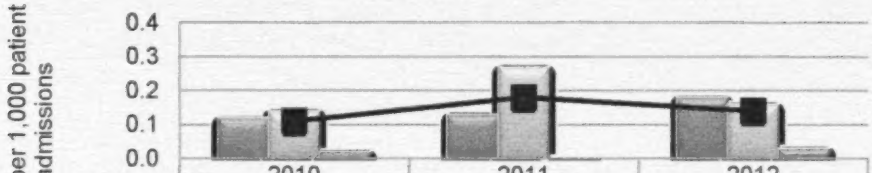
Case definition of carbapenem-resistant *Enterobacteriaceae* isolates

From January 1, 2010, to August 31, 2010, any patient with an *Enterobacteriaceae* that exhibited a minimum inhibitory concentration (MIC) value ≥2 μg/ml for any of three carbapenem antimicrobials (imipenem, meropenem, ertapenem); or a disk diffusion diameter ≤1mm was eligible for inclusion.

From September 1, 2010, to December 31, 2012, the MIC for ertapenem was decreased to ≥0.5 μg/ml and a disk diffusion diameter for any carbapenem ≤22 mm was considered eligible for inclusion.

The rates of carbapenem-resistant *Enterobacteriaceae* (CRE) have been measured since 2010 and have been low and stable, with 0.11 infections per 1,000 patient admissions in 2010 and 0.14 infections per 1,000 admissions in 2012, with higher rates in the Western and Central regions and lower rates in the Eastern region (**Figure 4**).

FIGURE 4. National and regional carbapenem-resistant *Enterobacteriaceae* (CRE) rates per 1,000 patient admissions, January 1, 2010 to December 31, 2012. N = 231



	2010	2011	2012
West	0.12	0.13	0.18
Central	0.14	0.27	0.16
East	0.02	0.00	0.03
Overall	0.11	0.18	0.14

Discussion

In Canada over the last few years, of the four antibiotic resistant organisms under surveillance, health care-associated *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus* have been gradually decreasing; vancomycin-resistant *Enterococci* infections have been low but are rising; and carbapenem-resistant *Enterobacteriaceae* infection remains low, with Western and Central rates consistently higher than Eastern rates.

Comparison of Canadian rates with international rates is difficult due to different definitions and analyses. For example, some countries report on MRSA bacteremia versus all types of MRSA. A number of countries report rates per 100,000 population, whereas these Canadian rates have been calculated using patient admissions to hospital. In addition, regional variation in rates is seen in countries and regions around the world. However, the overall trends seen in Canada are not dissimilar from trends observed elsewhere in the world.

Several limitations should be considered when interpreting the data presented here. First, the CNISP surveillance data is likely an underestimate as it does not represent the total number of inpatients in Canada with these infections. These data can only tell us about inpatients who have been tested and diagnosed, and not those who remain untested and undiagnosed. Cases identified in outpatient settings such as emergency departments and clinics are not captured by this surveillance system. Participating hospitals are not necessarily representative of all Canadian hospitals; for example, they tend to be large, tertiary acute care centres located in major cities. Antibiotic prescribing practices and implementation of infection prevention, and control measures may vary across hospitals, but because this surveillance system does not collect data regarding these factors, it is not possible to correlate them with the occurrence of these infections. And, as always, these results are subject to change as new data are made available.

Antimicrobial resistance will continue to challenge the health of Canadians and of people around the world for some time to come. Surveillance will help document the progress we continue to make in curbing it.

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Conflict of interest

None.

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Antibiotic recommendations of office-based physicians, 2007–2011

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Abstract

Objective: To describe patterns of antibiotic recommendations by office-based physicians from five regions in Canada between 2007 and 2011.

Methods: Values were estimated based on quarterly data from a sample of approximately 652 physicians stratified by region and specialty. For four consecutive quarters, each physician maintained a practice diary describing information on every patient visit during a randomly selected 48-hour period. This information was then extrapolated using a projection factor to estimate prescriptions by all physicians across Canada.

Results: Over the five-year surveillance period, physicians saw patients for almost 1.5 billion diagnoses with approximately 120 million antimicrobial recommendations. In 2011 alone, 289 million clinical diagnoses were made of which 8% resulted in an antimicrobial being recommended. The majority of these (51%) were for the treatment of diseases of the respiratory system, 14% for infections of the urinary tract, and 11% for diseases of skin and subcutaneous tissue. Antimicrobial recommendations were highest for patients in the age groups of 0–2, 3–9, and 65 or older. Antimicrobial recommendation rates generally decreased between 2007 and 2011 except for diseases of the genitourinary system and diseases of the ear that remained stable. Overall, the most commonly recommended antimicrobials included macrolides, penicillins with extended spectrum, and fluoroquinolones. Although not as common, there was a 42% increase in the number of physician recommendations for third generation cephalosporins.

Conclusion: With the exception of third generation cephalosporins, the percentage of antimicrobial recommendations by office-based physicians in Canada remained stable or decreased between 2007 and 2011. Provincial differences were observed in the antimicrobial recommendations and rates, with the Atlantic region and Québec having higher rates of antimicrobial recommendations compared to the overall national level.

Introduction

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) monitors trends in antimicrobial use and antimicrobial resistance in selected bacterial organisms from human, animal and food sources across Canada. The Program is based on several representative and methodologically unified surveillance components that can be linked to examine the relationship between antimicrobials used in food animals and humans, and the associated health impacts. This information supports: (i) the creation of evidence-based policies to control antimicrobial use in hospital, community, and agricultural settings, and thus prolong the effectiveness of these drugs; and (ii) the identification of appropriate

measures to contain the emergence and spread of resistant bacteria between animals, food, and people in Canada.
The human antimicrobial use surveillance reports are published on a regular basis to provide a national overview of current antimicrobial use practices in Canada annually, to enable comparisons and to support formulary and stewardship development. The objective of this paper is to summarize the most recent CIPARS report that describes patterns of antibiotic recommendations by office-based physicians from five regions in Canada between 2007 and 2011 (1).

Methods

The Canadian Disease and Therapeutic Index (CDTI) dataset is purchased by the Public Health Agency of Canada from IMS Health Canada Inc. This dataset provides information about the patterns and treatments of disease encountered by office-based physicians from five regions: Atlantic (New Brunswick, Newfoundland and Labrador, Nova Scotia, and Prince Edward Island), Québec, Ontario, the Prairies (Alberta, Manitoba, and Saskatchewan), and British Columbia. Values are estimated based on quarterly data from a sample of approximately 652 physicians stratified by region and specialty. For four consecutive quarters, each physician maintains a practice diary describing information on every patient visit during a randomly selected 48-hour period. This information is then extrapolated using a projection factor to estimate the "universe" comprised of approximately 52,959 physicians, roughly representing all Canadian data.

The information contained in this analysis is for antimicrobials for which a physician has provided a recommendation or prescription, and does not represent actual prescriptions dispensed by pharmacists or consumed by the patient. This data does not include patient visits to a primary care nurse, and diagnosis visits do not translate into the total number of patients, as some patients visited multiple times for the same reason or were diagnosed with multiple diseases. Due to the methods of data collection, sample size is sometimes considered too small for decision making. However, information is still included in this analysis to provide a view of practices which may require further study.

Results

Over the five-year surveillance period (2007–2011) physicians saw patients for almost 1.5 billion diagnoses and provided a total of approximately 121 million antimicrobial recommendations(1). In 2011, a total of 289 million clinical diagnoses were made of which 8% resulted in an antimicrobial recommendation (**Table 1**). During that year, out of all the antimicrobials recommended by office-based physicians, 51.3% were for treatment of diseases of the respiratory system followed by infections of the urinary tract (14.5%) and diseases of the skin and subcutaneous tissue (11.3%)

TABLE 1. Total number of office-based diagnoses, diagnosis rate, total number of antimicrobial recommendations, antimicrobial recommendation rate, and percentage of diagnoses with antimicrobial recommendations by office-based physicians in Canada, by diagnostic class, 2011

Diagnostic class	Total diagnoses	Total diagnoses / 10,000 inhabitants	Antimicrobial recommendations (N)	Total antimicrobial recommendations / 10,000 inhabitants	Percentage diagnoses with antimicrobial recommendations
Complications of pregnancy, childbirth, and puerperal	1,044,850	302	17,180	5	1.6
Congenital anomalies	925,330	267	21,290	6	2.3
Diseases of blood/blood-forming organs	2,593,490	749	45,160	13	1.7
Diseases of skin and subcutaneous tissue	21,784,200	6,295	2,551,830	737	11.7
Diseases of the central nervous system	10,591,580	3,061	148,900	43	1.4
Diseases of the circulatory system	33,884,750	9,791	62,510	18	0.2
Diseases of the ear	7,627,370	2,204	2,232,080	645	29.3
Diseases of the gastrointestinal system	1,674,160	484	107,900	31	6.4
Diseases of the genitourinary system	12,878,470	3,721	821,180	237	6.4
Diseases of the respiratory system	37,079,860	10,715	11,628,520	3,360	31.4
Endocrine, nutritional, metabolic, and immunity diseases	28,537,420	8,246	62,310	18	0.2
Infections of the urinary tract	6,951,220	2,009	3,285,390	949	47.3
Injuries and poisonings	11,575,360	3,345	317,020	92	2.7
Musculoskeletal diseases	28,086,920	8,116	136,030	39	0.5
Neoplasms	7,124,130	2,059	93,740	27	1.3
Other diseases of the digestive system	17,401,060	5,028	684,730	198	3.9
Perinatal conditions	438,380	127	14,540	4	3.3
Supplementary classifications	37,076,290	10,714	77,420	22	0.2
Symptoms and ill-defined conditions	21,771,660	6,291	359,500	104	1.7
Total	**289,046,500**	**83,524**	**22,667,230**	**6,550**	**7.8**

Antimicrobials were recommended to all age groups in 2011, with proportionally higher recommendation rates to patients in the age group 0–2 years (12 antimicrobial recommendations per 10 inhabitants); 3–9 years (9 antimicrobial recommendations per 10 inhabitants); and 60–64 years, and 65 years of age or older (7 antimicrobial recommendations per 10 inhabitants for each age group) (**Table 2**).

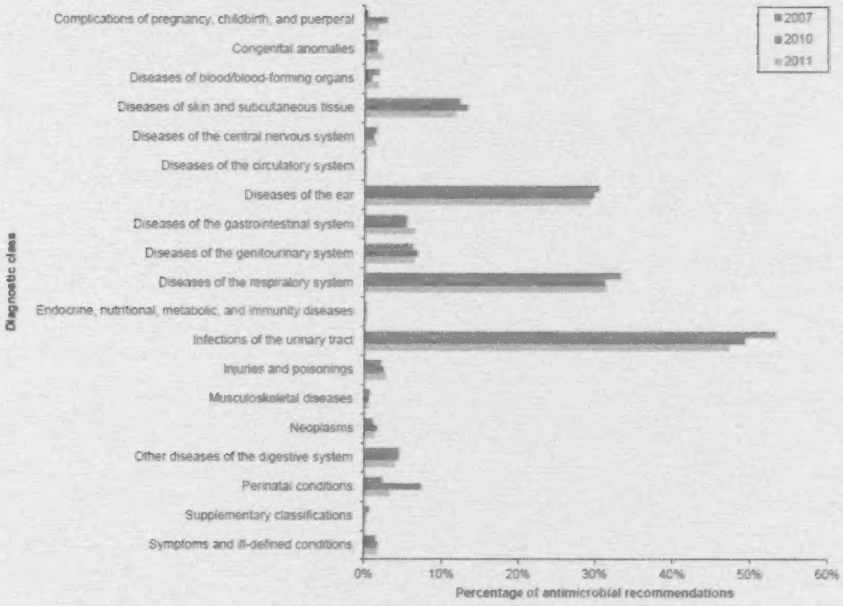
TABLE 2. Diagnosis rate, antimicrobial recommendation rate and percentage of diagnosis with antimicrobial recommendation provided by office-based physicians in Canada, by age group and by gender, 2011

Demographics: age (year) or gender	Number of diagnoses / 10 inhabitants[1]	Antimicrobial recommendations / 10 inhabitants[2]	Percentage of diagnoses with antimicrobial recommendations
Age			
0 to 2	123	12	9.7
3 to 9	52	9	16.5
10 to 19	42	6	13.0
20 to 39	59	6	10.7
40 to 59	81	5	6.6
60 to 64	122	7	5.5
65 or older	152	7	4.9
Gender			
Female	93	7	7.7
Male	71	6	8.0

[1]Diagnosis does not represent the number of times a person visits, but represents every time a diagnosis is provided; if a person presents multiple diseases each individual disease/diagnosis is recorded separately.
[2]Data does not represent actual prescriptions dispensed by pharmacists or products consumed by the patient, as information on patient compliance was not available.

For the most part, the percentage of antimicrobial recommendations by office-based physicians in Canada remained stable or decreased between 2007 and 2011 (**Figure 1**). Slight increases were seen related to complications of pregnancy, childbirth, and puerperal; congenital anomalies; diseases of the gastrointestinal system; injuries and poisonings; and perinatal conditions.

FIGURE 1. Percentage of diagnoses that received an antimicrobial recommendation by office-based physicians in Canada, 2007, 2010, and 2011



The most commonly recommended antimicrobials in 2011 were the macrolides (1,638 recommendations per 10,000 inhabitants), penicillins with extended spectrum (1,504 recommendations per 10,000 inhabitants), and the fluoroquinolones (1,202 recommendations per 10,000 inhabitants). However, high increases in the number of physician recommendations were observed for third generation cephalosporins (a 42% increase compared to 2007) due to an increase in recommendations for treatment of diseases of the respiratory system, diseases of the genitourinary system, and infections of the urinary tract.

Provincial variation in the total number of antimicrobial recommendations per 10,000 inhabitants was observed, with the Atlantic region (7,101 recommendations per 10,000 inhabitants) and Québec (8,268 recommendations per 10,000 inhabitants) having the highest rates compared to the overall national level. Rates of diagnoses and antimicrobial recommendations per 10,000 inhabitants varied depending upon the province and disease of treatment. Provincial preferences for antimicrobial of choice for treatment of disease were also observed (**Table 3**).

TABLE 3. Diagnosis rate, antimicrobial recommendation rate and percentage of diagnoses with antimicrobial recommendations provided by office-based physicians in Canada, by diagnostic class and by province/region, 2011

Diagnostic class	Province / region	Number of diagnoses / 10,000 inhabitants[1]	Antimicrobial recommendations / 10,000 inhabitants[2]	Percentage of diagnoses with antimicrobial recommendations
Complications of pregnancy, childbirth, and puerperal	British Columbia	350	NAS[3]	NAS
	Prairies[4]	303	3	1.1
	Ontario	271	NAS	NAS
	Quebec	330	19	5.7
	Atlantic[5]	298	NAS	NAS
	Total	302	5	1.6
Congenital anomalies	British Columbia	374	10	2.7
	Prairies	265	13	4.7
	Ontario	171	5	2.9
	Quebec	296	NAS	NAS
	Atlantic	530	10	1.9
	Total	267	6	2.3
Diseases of blood/blood-forming organs	British Columbia	715	NAS	NAS
	Prairies	665	12	1.8
	Ontario	744	20	2.7
	Quebec	707	13	1.9
	Atlantic	1,242	NAS	NAS
	Total	749	13	1.7
Diseases of skin and subcutaneous tissue	British Columbia	7,602	820	10.8
	Prairies	6,061	706	11.6
	Ontario	5,866	792	13.5
	Quebec	6,399	664	10.4
	Atlantic	6,741	631	9.4
	Total	6,295	737	11.7
Diseases of the central nervous system	British Columbia	3,472	73	2.1
	Prairies	2,440	33	1.3
	Ontario	3,297	39	1.2
	Quebec	3,020	37	1.2
	Atlantic	2,811	57	2.0
	Total	3,061	43	1.4
Diseases of the circulatory system	British Columbia	9,503	48	0.5

Prairies	9,231	5	0.0
Ontario	9,479	19	0.2
Quebec	1,037	8	0.8
Atlantic	12,081	24	0.2
Total	9,792	18	0.2

[1]Diagnosis does not represent the number of times a person visits, but represents every time a diagnosis is provided; if a person presents with multiple diseases each individual disease/diagnosis is recorded separately.
[2]Data does not represent actual prescriptions dispensed by pharmacists or products consumed by the patient, as information on patient compliance was not available.
[3]NAS = no antimicrobials suggested (recommended).
[4]The Prairies include the provinces of Alberta, Saskatchewan, and Manitoba.
[5]The Atlantic region includes the provinces of New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador.

TABLE 3 (continued). Diagnosis rate, antimicrobial recommendation rate and percentage of diagnoses with antimicrobial recommendations provided by office-based physicians in Canada, by diagnostic class and by province/region, 2011

Diagnostic class	Province / region	Number of diagnoses / 10,000 inhabitants[1]	Antimicrobial recommendations / 10,000 inhabitants[2]	Percentage of diagnoses with antimicrobial recommendations
Diseases of the ear	British Columbia	2,285	349	15.3
	Prairies[4]	1,628	460	28.2
	Ontario	1,708	514	30.1
	Quebec	3,123	1,168	37.4
	Atlantic[5]	3,348	702	21.0
	Total	2,204	645	29.3
Diseases of the gastrointestinal system	British Columbia	452	53	11.6
	Prairies	521	9	1.7
	Ontario	461	29	6.4
	Quebec	530	28	5.3
	Atlantic	445	69	15.6
	Total	484	31	6.4
Diseases of the genitourinary system	British Columbia	3,646	207	5.7
	Prairies	3,500	252	7.2
	Ontario	3,606	218	6.0
	Quebec	3,815	277	7.3
	Atlantic	4,957	243	4.9
	Total	3,722	237	6.4
Diseases of the respiratory system	British Columbia	9,699	2,649	27.3
	Prairies	10,193	3,307	32.4
	Ontario	9,687	3,000	31.0
	Quebec	13,044	4,377	33.6
	Atlantic	12,504	3,641	29.1
	Total	10,715	3,360	31.4
Endocrine, nutritional, metabolic, and immunity diseases	British Columbia	7,353	NAS[3]	NAS
	Prairies	6,940	14	0.2
	Ontario	8,557	23	0.3
	Quebec	8,477	28	0.3
	Atlantic	11,215	5	< 0.1
	Total	8,247	18	0.2
Infections of the urinary tract	British Columbia	2,241	982	43.8
	Prairies	1,886	825	43.8

	Ontario	1,869	855	45.7
	Quebec	1,891	1,143	60.5
	Atlantic	3,164	1,134	35.8
	Total	2,009	949	47.3

[1]Diagnosis does not represent the number of times a person visits, but represents every time a diagnosis is provided; if a person presents with multiple diseases each individual disease/diagnosis is recorded separately.
[2]Data does not represent actual prescriptions dispensed by pharmacists or products consumed by the patient, as information on patient compliance was not available.
[3]NAS = no antimicrobials suggested (recommended).
[4]The Prairies include the provinces of Alberta, Saskatchewan, and Manitoba.
[5]The Atlantic region includes the provinces of New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador.

TABLE 3 (continued). Diagnosis rate, antimicrobial recommendation rate and percentage of diagnoses with antimicrobial recommendations provided by office-based physicians in Canada, by diagnostic class and by province/region, 2011

Diagnostic class	Province / region	Number of diagnoses / 10,000 inhabitants[1]	Antimicrobial recommendations / 10,000 inhabitants[2]	Percentage of diagnoses with antimicrobial recommendations
Injuries and poisonings	British Columbia	5,400	99	1.8
	Prairies[4]	3,446	93	2.7
	Ontario	2,864	94	3.3
	Quebec	3,221	90	2.8
	Atlantic[5]	2,398	73	3.0
	Total	3,345	92	2.7
Musculoskeletal diseases	British Columbia	8,402	4	< 0.1
	Prairies	8,748	53	0.6
	Ontario	7,911	56	0.7
	Quebec	6,804	13	0.2
	Atlantic	11,928	69	0.6
	Total	8,116	39	0.5
Neoplasms	British Columbia	2,012	10	0.5
	Prairies	1,630	3	0.2
	Ontario	1,840	8	0.5
	Quebec	2,645	95	3.6
	Atlantic	2,614	NAS[3]	NAS
	Total	2,059	27	1.3
Other diseases of the digestive system	British Columbia	4,925	237	4.8
	Prairies	5,460	138	2.5
	Ontario	4,547	214	4.7
	Quebec	4,962	224	4.5
	Atlantic	7,311	106	1.5
	Total	5,028	198	3.9
Perinatal conditions	British Columbia	123	NAS	NAS
	Prairies	154	16	10.1
	Ontario	151	NAS	NAS
	Quebec	96	6	6.5
	Atlantic	35	NAS	NAS
	Total	127	4	3.3
Supplementary classifications	British Columbia	10,174	12	0.1
	Prairies	12,776	9	0.1
	Ontario	10,851	24	0.2
	Quebec	9,323	37	0.4
	Atlantic	10,867	21	0.2
	Total	10,714	22	0.2
Symptoms and ill-defined	British Columbia	6,427	97	1.5

conditions	Prairies	5,819	68	1.2
	Ontario	6,666	123	1.9
	Quebec	4,792	41	0.9
	Atlantic	10,502	315	3.0
	Total	6,291	104	1.7

[1]Diagnosis does not represent the number of times a person visits, but represents every time a diagnosis is provided; if a person presents with multiple diseases each individual disease diagnosis is recorded separately.
[2]Data does not represent actual prescriptions dispensed by pharmacists or products consumed by the patient, as information on patient compliance was not available.
[3]NAS = no antimicrobials suggested (recommended).
[4]The Prairies include the provinces of Alberta, Saskatchewan, and Manitoba.
[5]The Atlantic region includes the provinces of New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador.

Discussion

Eight percent of clinical diagnoses provided by office-based physicians resulted in an antimicrobial being recommended in 2011. Of these, 51% were for the treatment of diseases of the respiratory system, followed by 14% for infections of the urinary tract, and 11% for diseases of skin and subcutaneous tissue. Antimicrobial recommendations were highest for patients in the age groups of 0–2 years, 3–9 years, and 65 years or older. Antimicrobial recommendation rates decreased between 2007 and 2011 for diseases of the ear, the respiratory system, infections of the urinary tract, and diseases of the skin and subcutaneous tissue, while the rates for diseases of the genitourinary system remained stable.

Overall, the most commonly recommended antimicrobials included macrolides, penicillins with extended spectrum and fluoroquinolones. Provincial differences were observed in the antimicrobial recommendation rates and antimicrobial selected for treatment, with the Atlantic region and Québec having higher rates of antimicrobial recommendations compared to the national levels. British Columbia had the lowest rate of antimicrobial recommendations for diseases of the respiratory system, while Québec and the Atlantic region had the highest for diseases of the ear. The Prairies had the lowest rate of antimicrobial recommendations for infections of the urinary tract, but did observe an increase in these between 2010 and 2011. A similar rate of antimicrobial recommendations across the country was observed for diseases of the genitourinary system, while decreases in recommendations were observed across the country for diseases of the skin and subcutaneous tissue.

There are several limitations and caveats within the CDTI dataset. The drugs listed are those that the physician has written or recommended and do not represent actual prescriptions dispensed by pharmacists or products consumed by the patient, as information on patient compliance was not available. The data do not include patient visits to a primary care nurse, and diagnosis visits do not translate into number of patients as some patients may have visited multiple times for the same reason or were diagnosed with multiple diseases.

The appearance of a drug may include samples that do not necessarily tie to a prescription dispensed as physicians list all suggested treatments. Physicians also record drugs "previously ordered and continued" for the diagnosis, which would not necessarily tie to a prescription dispensed. In addition, some drug therapy and diagnosis is under-represented due to self-medication (i.e., over-the-counter products). Sample size is sometimes considered too small for decision making; however, these have been included for information purposes only and reliability of the data is dependent on sampling error, so caution should be taken when interpreting those disease categories with a small sample size. Data are only available at the regional level, where fluctuations may be more or less obvious and specific information for individual provinces could not be determined.
Antimicrobial resistance will continue to challenge the health of Canadians and those around the world for some time to come. Antibiotic use surveillance will help document the progress we have made in curbing it and the impact these changes might have had on overall antibiotic resistance.

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Conflict of interest

None.

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Disclaimer

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Antibiotic purchasing by Canadian hospitals, 2007–2011

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Abstract

Objective: To describe patterns of antibiotic purchasing by Canadian hospitals from five regions in Canada between 2007 and 2011.

Methods: The Canadian Drugstore and Hospital Purchases Audit (CDH) dataset measures the dollar value and unit volume of pharmaceutical products from over 700 hospitals and is extrapolated to represent purchases by more than 800 hospitals in Canada. General population information was used for developing the rates of purchasing with a primary focus on unit volume.

Results: In 2011, there was a 7% increase in total antibiotics purchased by Canadian hospitals compared to 2010, with slight increases in the purchasing levels for oral (8% increase) and parenteral (3% increase) antibiotics. Antibiotics considered of very high importance to human medicine (Category I) continued to represent a high proportion of the total antibiotics used in hospitals in 2011. Overall, consumption of antibiotics was highest in Manitoba at 2.61 doses per 1,000 inhabitants per day (DID), while Ontario had the lowest levels of consumption (1.26 DID). New Brunswick had the highest proportion of Category I consumption (43%, 0.62/1.43 DID) for 2011, driven by higher levels of fluoroquinolones consumed in that province.

Conclusion: Canadian hospitals have purchased an increasing number of antibiotics and are consuming slightly more oral and parenteral antibiotics. Overall, consumption was highest in Manitoba and total cost was highest in British Columbia. Ontario had the lowest level of consumption of anitbiotics and the lowest overall cost.

Introduction

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) monitors trends in antimicrobial use and antimicrobial resistance in selected bacterial organisms from human, animal, and food sources across Canada. The Program is based on several representative and methodologically unified surveillance components that can be linked to examine the relationship between antibiotics used in food animals and humans, and the associated health impacts. This information supports: (i) the creation of evidence-based policies to control antimicrobial use in hospital, community, and agricultural settings, and thus prolong the effectiveness of these drugs; and (ii) the identification of appropriate measures to contain the emergence and spread of resistant bacteria between animals, food, and people in Canada.

The human antimicrobial use surveillance reports are published on a regular basis to provide a national overview of current antibiotic use practices in Canada annually, to enable comparisons and to support formulary and stewardship development. The objective this paper is to describe patterns of antibiotic purchasing by Canadian hospitals from five regions in Canada between 2007 and 2011. This information is based on the most recent CIPARS Report which is available online. (1)

Methods

The Canadian Drugstore and Hospital Purchases Audit (CDH) dataset is purchased by the Public Health Agency of Canada from IMS Health Canada Inc. This dataset measures the dollar value and unit volume of pharmaceutical products purchased by nearly all Canadian hospitals excluding those in the Yukon, Northwest Territories, and Nunavut. Information was collected from over 700 hospitals and extrapolated to represent purchases by more than 800 hospitals in Canada. The provinces of Prince Edward Island, and Newfoundland and Labrador were grouped due to the small volume of hospital purchases within each province. Hospital patient days and number of hospital beds were not available for this data; general population information was used for developing the rates of purchasing. In this paper, the term "consumption" is used to reflect hospital purchases.

Results

In 2011, there was a 27% increase in the total mass of antibiotics purchased compared to 2001 (34,958.30 kg purchased in 2001 versus 44,406.35 kg in 2011). However, the total number of defined daily doses per 1,000 inhabitant-days (DID) have remained fairly stable for both oral and parenteral antibiotics since 2001 (**Table 1** and **Table 2**). Slight increases were observed among the oral (8%) and parenteral (3%) antibiotics in 2011 compared to 2010, driven by slight increases among the tetracyclines (25%), combinations of penicillins, including β-lactamase inhibitors (25%), and macrolides (8%) (**Table 1**).

TABLE 1. Defined daily doses per 1,000 inhabitant-days for oral antibiotics purchased by hospitals in Canada, 2001–2011

	ATC[1] Class and antimicrobial	DDDs[2] / 1,000 inhabitant-days										
		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
I[3]	**β-lactamase inhibitors (J01CR)** Amoxicillin and enzyme inhibitor	0.02	0.02	0.03	0.03	0.04	0.04	0.03	0.03	0.04	0.04	0.05
	Third-generation cephalosporins (J01DD) Cefixime	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	Fluoroquinolones (J01MA) moxifloxacin, gatifloxacin, gemifloxacin	0.22	0.22	0.24	0.24	0.23	0.23	0.23	0.22	0.23	0.20	0.20
	Imidazole (J01XD) Metronidazole	0.04	0.03	0.04	0.04	0.04	0.04	0.04	0.04	0.03	0.03	0.03
II	**Penicillins with extended spectrum (J01CA)** pivmecillinam	0.11	0.11	0.10	0.09	0.10	0.09	0.08	0.08	0.08	0.09	0.09
	β-lactamase sensitive penicillins (J01CE) Penicillin G, penicillin V	0.02	0.03	0.03	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.02
	β-lactamase resistant penicillins (J01CF) Cloxacillin	0.03	0.02	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01
	First-generation cephalosporins (J01DB) Cephalexin, cefadroxil	0.05	0.05	0.05	0.05	0.06	0.07	0.05	0.05	0.05	0.04	0.05
	Second-generation cephalosporins (J01DC) Cefaclor, cefprozil, cefuroxime axetil	0.07	0.05	0.05	0.05	0.04	0.04	0.04	0.04	0.04	0.03	0.04
	trimethoprim, including derivatives (J01EE) and trimethoprim	0.09	0.07	0.08	0.07	0.07	0.07	0.07	0.06	0.06	0.06	0.06
	Macrolides (J01FA) spiramycin, telithromycin	0.13	0.13	0.14	0.12	0.13	0.12	0.13	0.13	0.14	0.12	0.13
	Lincosamides (J01FF) Clindamycin	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.01	0.01
III	**Tetracyclines (J01AA)** demeclocycline	0.06	0.05	0.05	0.06	0.05	0.06	0.08	0.12	0.08	0.08	0.10
	Nitrofuran derivatives (J01XE) Nitrofurantoin	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
	Total (J01)	**0.89**	**0.84**	**0.97**	**0.96**	**0.86**	**0.86**	**0.83**	**0.85**	**0.84**	**0.78**	**0.84**

[1] ATC = Anatomical Therapeutic Chemical

[2] DDDs = defined daily doses

[3] Roman numerals I–III indicate the ranking of antibiotics based on importance in human medicine as outlined by the Veterinary Drugs Directorate.

Antibiotics considered of very high importance to human medicine (Category I) represent 35% and 34% of the total DID of oral and parenteral antibiotics purchased by hospitals in 2011, respectively (**Table 1**

and **Table 2**). This is an increase since 2001, when these antibiotics among the oral form represented 33% and parenteral drugs represented 28% of purchases.

Similarly, increased consumption of parenteral drugs was mainly due to increases in combinations of penicillins, including β-lactamase inhibitors (20%) and third generation cephalosporins (14%) (**Table 2**).

TABLE 2. Defined daily doses per 1,000 inhabitant-days for parenteral antibiotics purchased by hospitals in Canada, 2001–2011

	ATC[1] Class and antimicrobial	DDDs[2] per 1,000 inhabitant-days										
		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
P	**β-lactamase inhibitors (J01CR)** enzyme inhibitor	0.02	0.02	0.03	0.02	0.03	0.03	0.04	0.04	0.05	0.05	0.06
	Third-generation cephalosporins (J01DD) Cefotaxime, ceftazidime, ceftizoxime, ceftriaxone	0.03	0.05	0.06	0.06	0.07	0.07	0.06	0.07	0.08	0.07	0.08
	Fourth-generation cephalosporins (J01DE) Cefepime, ceftobiprole	< 0.01	< 0.01	0.01	0.03	0.02	0.01	0.01	< 0.01	< 0.01	< 0.01	< 0.01
	Carbapenems (J01DH) Doripenem, ertapenem, imipenem, meropenem	0.01	0.03	0.03	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.04
	Fluoroquinolones (J01MA) moxifloxacin	0.05	0.06	0.06	0.07	0.07	0.08	0.06	0.06	0.06	0.05	0.05
	Glycopeptides (J01XA) Vancomycin	0.04	0.04	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.02	0.02
	Imidazole (J01XD) Metronidazole	0.06	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
II	**Penicillins with extended spectrum (J01CA)** Ampicillin, pivampicillin	0.07	0.06	0.05	0.05	0.05	0.05	0.05	0.05	0.04	0.04	0.04
	β-lactamase sensitive penicillins (J01CE) Penicillin G	0.21	0.19	0.22	0.27	0.28	0.28	0.26	0.27	0.26	0.25	0.25
	β-lactamase resistant penicillins (J01CF) Cloxacillin	0.05	0.04	0.05	0.04	0.04	0.04	0.04	0.04	0.05	0.04	0.04
	First-generation cephalosporins (J01DB) Cefazolin, cephalothin	0.12	0.12	0.12	0.12	0.12	0.11	0.12	0.12	0.13	0.12	0.12
	Second-generation cephalosporins (J01DC) Cefotetan, cefoxitin, cefuroxime	0.04	0.04	0.03	0.02	0.01	0.01	0.01	0.01	0.01	< 0.01	< 0.01
	Macrolides (J01FA) Azithromycin, erythromycin	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	Lincosamides (J01FF) Clindamycin	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.03
	Aminoglycosides (J01GB) Amikacin, gentamicin, netilmicin, tobramycin	0.06	0.05	0.03	0.02	0.03	0.05	0.05	0.04	0.04	0.04	0.03
	Total (J01)	**0.78**	**0.76**	**0.76**	**0.77**	**0.79**	**0.83**	**0.80**	**0.79**	**0.82**	**0.77**	**0.79**

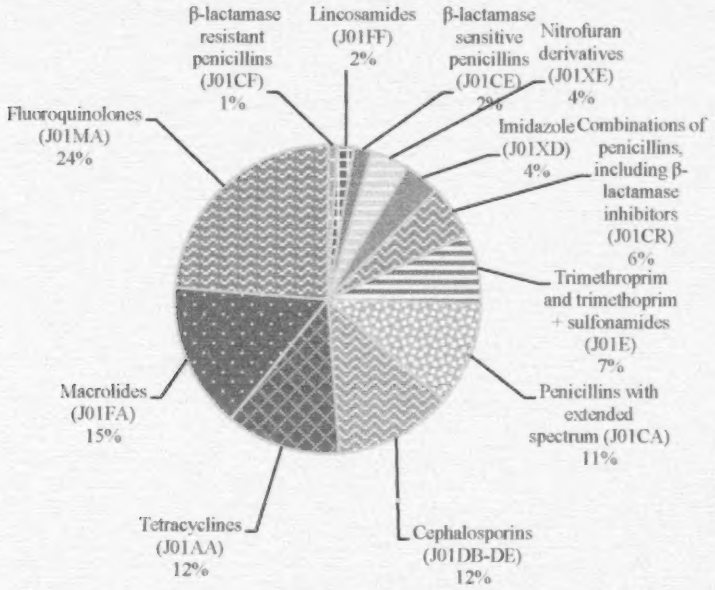
[1] ATC = Anatomical Therapeutic Chemical

[2] DDDs = defined daily doses

[3] Roman numerals I and II indicate the ranking of antibiotics based on importance in human medicine as outlined by the Veterinary Drugs Directorate.

Fluoroquinolones represent the largest group of oral antibiotic agents consumed (24%), followed by macrolides (15%), tetracyclines (12%), cephalosporins (12%), and penicillins with extended spectrum (11%) (**Figure 1**).

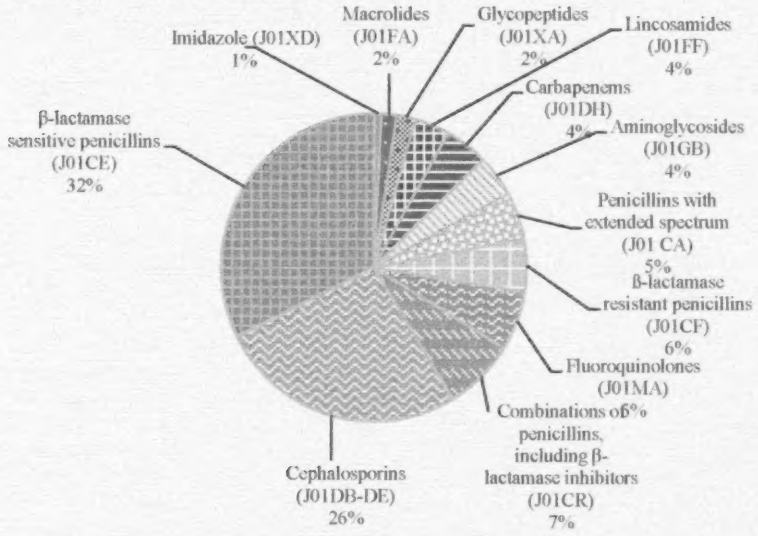
FIGURE 1. Percentages of total number of defined daily doses per 1,000 inhabitant-days for oral antibiotics purchased by hospitals in Canada, 2011



Note: Alphanumeric codes in parentheses represent Anatomical Therapeutic Chemical classes of antibiotics.

β-lactamase sensitive penicillins (penicillin G and penicillin V) (32%) and cephalosporins (26%) are the largest groups of parenteral antibiotics purchased by Canadian hospitals (**Figure 2**).

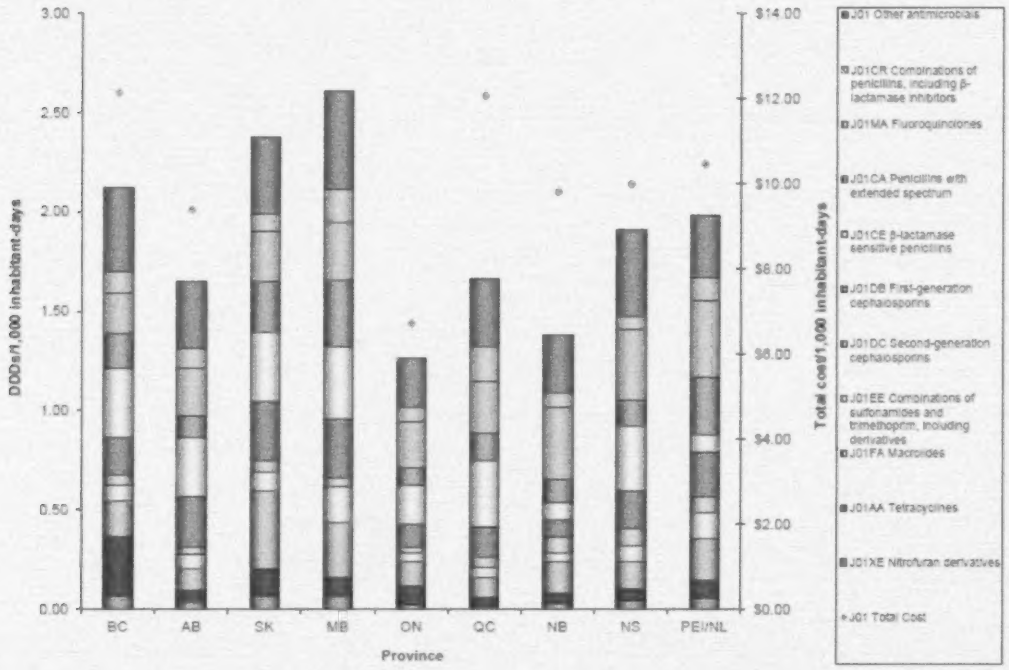
FIGURE 2. Percentages of total number of defined daily doses per 1,000 inhabitant-days for parenteral antibiotics purchased by hospitals in Canada, 2011



Note: Alphanumeric codes in parentheses represent Anatomical Therapeutic Chemical classes of antibiotics.

In 2011, differences in total consumption and total cost in dollars (per 1,000 inhabitant-days) for antibiotic purchases by Canadian hospitals were observed across Canada. Overall, consumption of antibiotics was highest in Manitoba (2.61 DID), whereas Ontario had the lowest levels reported (1.26 DID) (**Figure 3**). Total cost associated with antimicrobial purchases for hospital use was highest in British Columbia ($12.13 per 1,000 inhabitant-days), while the lowest levels were observed in Ontario ($6.72 per 1,000 inhabitant-days) (**Figure 3**).

FIGURE 3. Total consumption (DDDs/1,000 inhabitant-days) and total cost of oral and parenteral antibiotics purchased by hospitals in Canadian provinces, 2011



Note: Alphanumeric codes in text box represent Anatomical Therapeutic Chemical classes of antibiotics.

Discussion

In 2011, there was a 27% (9,448.05 kg) increase in total antibiotics purchased by Canadian hospitals compared to 2001, with slight increases in the levels of consumption for oral (8% increase) and parenteral (3% increase) antibiotics. Antibiotics considered of very high importance to human medicine (Category I) continued to represent a high proportion (0.56/1.62 DID) of the total antibiotics used in hospitals in 2011.

Overall, consumption (DID) of antibiotics was highest in Manitoba (2.61 DID), while total cost in dollars (per 1,000 inhabitant-days) was highest in British Columbia ($12.13 per 1,000 inhabitant-days). Ontario on the other hand had the lowest levels of consumption (1.26 DID) and the lowest overall cost ($6.72 per 1,000 inhabitant-days). New Brunswick had the highest proportion of Category I consumption (43%, 0.62/1.43 DID) for 2011, driven by higher levels of fluoroquinolones consumed in that province.

There are several limitations and caveats within the CDH dataset. The data are estimated and are not census data; also, there is limited tracking of specific niche markets (due to low volume and/or unique distribution). In addition, a small number of products may be excluded due to confidentiality (e.g., if they

are sold only in one outlet). Some data may be excluded to reflect true market trends (i.e., large stockpiling transactions that occur prior to a potential epidemic) and direct sales for a specific manufacturer may not be available leading to underestimation of a product (higher incidence in hospital than in drug store purchases).

The provinces of Prince Edward Island, and Newfoundland and Labrador were grouped due to the small volume of purchases within each province. Changes made to the databases are made to the last 72 months only; outside the six-year period it is considered a closed dataset as updates cannot be made. Hospital patient days and number of hospital beds were not available for this data; general population information was used for developing rates of purchasing.

Antimicrobial resistance will continue to challenge the health of Canadians and of people around the world for some time to come. Surveillance of antibiotic use will help document the progress we continue to make in curbing it.

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Conflict of interest

None.

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Disclaimer

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Canadian integrated program for antimicrobial resistance surveillance: Retail food highlights, 2003–2012

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Abstract

Background: The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is a collaborative, integrated program designed to track antimicrobial resistance (AMR) among enteric bacteria isolated from various livestock commodities along the food-producing continuum ("farm to fork") and in humans.

Objective: To provide a summary of the prevalence and trends in AMR among select bacteria isolated from raw, fresh chicken, pork, and beef in 2012 at the retail food level and to link these data with other findings from CIPARS.

Methods: Meat samples were collected from randomly selected geographic areas across Canada weighted by population for subsequent isolation of bacteria and interpretation of the associated AMR profiles. *Salmonella*, *Campylobacter* and generic *Escherichia coli* (*E. coli*) were tested in chicken, and *E. coli* was tested in beef and pork. Data were analyzed for 2012 and temporal and regional trends were examined between 2003 and 2012 by province/region.

Results: Overall, resistance levels to *Salmonella* in retail chicken varied widely by region and year. For example, ceftiofur resistance to *Salmonella* in retail chicken was significantly lower in 2012 than in 2004 in Ontario and in Québec; however, among all regions sampled, resistance was significantly higher in 2012 compared to 2006. Across all regions sampled, resistance to *Campylobacter* in retail chicken was relatively low in 2012 (<16%) with the exception of tetracycline resistance. In 2012, ciprofloxacin resistance to *Campylobacter* in chicken declined in British Columbia but significantly increased in Ontario, compared to 2011. In 2012, β-lactam resistance to *E. coli* in retail beef remained low (≤1%) and was also relatively low comparable to previous years in pork.

Conclusion: In Canada, as is the case worldwide, there is evidence of resistance to medically important antimicrobials among bacteria from retail meats. Resistance among organisms isolated from poultry, beef, and pork at the retail food level is characterized by wide variation over time and across different regions.

Introduction

The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is a collaborative, integrated program designed to track antimicrobial resistance (AMR) among enteric bacteria isolated from various livestock commodities along the food-producing continuum ("farm to fork") and in humans. Specifically, the majority of the surveillance activities are strategically conducted at the farm, abattoir, and retail food levels, as well as in clinical isolates from animals and humans. Antimicrobials are frequently used in veterinary medicine and livestock production; some of the same antimicrobials, or close relatives, are also used in human medicine. All antimicrobial use in humans and animals can select for resistant

strains of bacteria; concerns are typically focused around uses that are, or are perceived to be, inappropriate as these unnecessarily add to the burden of resistance. The use of these important drugs in food animals (e.g., chickens, pigs, cattle) may pose a risk to public health through potential transfer of antimicrobial resistant organisms or resistance genes in food.

The *Retail Meat Surveillance* component of CIPARS provides data on antimicrobial resistance among select bacteria found in raw meat at the provincial/regional level. Retail food represents a logical sampling point for surveillance of AMR because it is the endpoint of food animal production, and thus is indicative of human exposure. Retail surveillance provides a measure of human exposure to resistant bacteria through consumption of fresh, raw (uncooked) meat products from selected commodities.

Annual CIPARS reports are published on a regular basis. The objective of these reports is to provide a summary of the prevalence and trends (temporal variations) in antimicrobial resistance in select bacterial species isolated from humans and the agri-food sector. In the 2012 surveillance year, the CIPARS Annual Report was refined to include multiple chapters released in succession to make the CIPARS data available to stakeholders in a more timely fashion (1). This article summarizes some of the notable retail meat findings of the most recent 2012 CIPARS Report and links these data with findings from other CIPARS surveillance components.

Methods

The commodities of interest for retail meat surveillance reported here were raw meat products most commonly consumed by Canadians. These commodities and the products sampled by CIPARS included poultry (chicken legs or wings [skin-on]), pork (chops), and beef (ground). Turkey (ground) was also added in 2012 but with only one year of surveillance, data were not included in this summary. The unit of analysis was the bacterial isolate recovered from raw meat. Bacteria of interest in chicken were the pathogens *Campylobacter* and *Salmonella*, and generic *Escherichia coli* (*E. coli*), as an indicator of AMR selection pressure and a reservoir of resistance genes. From beef and pork, given the low prevalence of *Campylobacter* and *Salmonella* in these commodities at retail as determined in earlier years of the Program, only *E. coli* was routinely cultured and then tested for antimicrobial susceptibility. Retail meat samples are submitted from randomly selected geographic areas (i.e., census divisions defined by Statistics Canada), weighted by population, in each participating province/region. In 2012, retail meat samples were collected on a weekly basis in Ontario and Québec, and every other week in British Columbia, Saskatchewan, and the Maritime provinces (New Brunswick, Nova Scotia, and Prince Edward Island).

Prevalence estimates, based on an expected yield of 100 isolates of each targeted bacteria per commodity per province/region per year, are used to determine the number of samples to be collected. As sampling was less frequent in British Columbia, Saskatchewan, and the Maritimes, the target of 100 isolates per year was not always achieved in those provinces/regions in a given year.

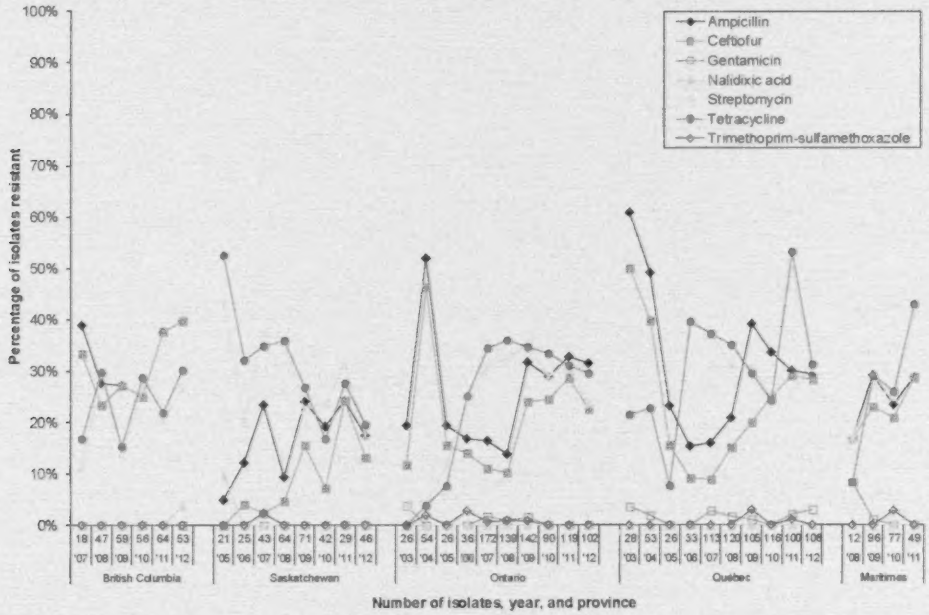
Resistance is reported based on Health Canada's Categorization of antimicrobial drugs (2): Category I (very high importance to human medicine), Category II (high importance to human medicine), and Category III (moderate importance to human medicine). Retail data were analyzed and results compared and integrated with the other components of CIPARS (e.g., farm, abattoir, and human) to provide a more complete picture of antimicrobial resistance in food-borne bacteria in Canada. Full details about CIPARS including sampling, laboratory and analytical methods are available in the Annual Reports (3).

Results

Chicken

Across all provinces sampled, the top three chicken *Salmonella* serovars were *S.* Heidelberg, *S.* Kentucky, and *S.* Enteritidis. All *S.* Enteritidis isolates were susceptible to all antimicrobials tested in 2012. No ciprofloxacin (Category I) resistance was observed in any serotype in 2012. Nalidixic acid (Category II) resistance was observed in two *S.* Kentucky isolates (4%) from British Columbia; previously nalidixic acid resistance had only been observed in two isolates from Saskatchewan in 2005 (**Figure 1**). Overall, Category I β-lactam (amoxicillin-clavulanic acid, ceftriaxone, ceftiofur) resistance levels (26%) remained similar to levels in 2011 (30%). Resistance to ceftiofur was significantly lower (23%) in 2012 than 2004 (46%) in Ontario. Although resistance to ceftiofur in Québec was significantly lower (28%) in 2012 than 2003 (50%), resistance was significantly higher in 2012 compared to 2006 (9%) (**Figure 1**).

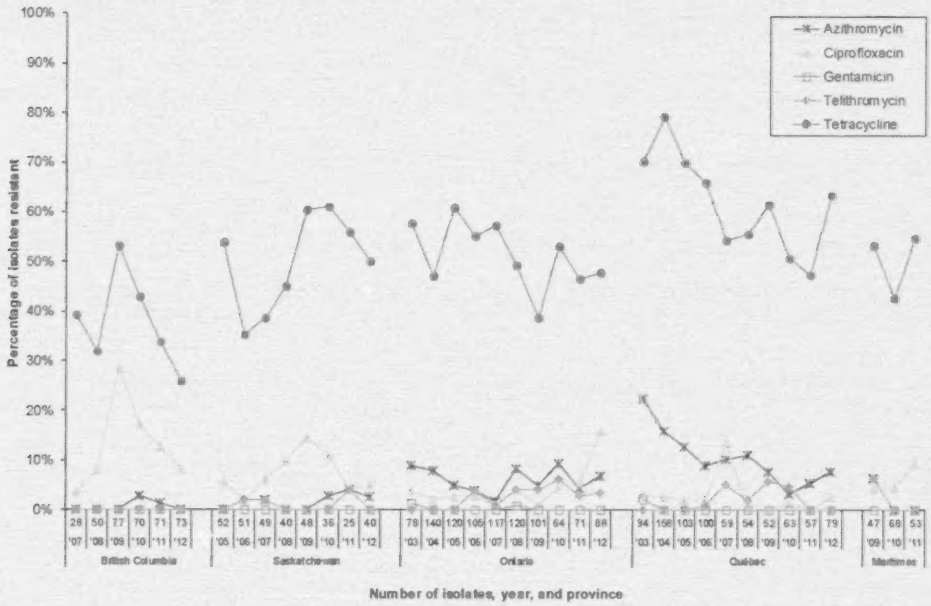
FIGURE 1. Temporal variation in resistance to selected antimicrobials in *Salmonella* isolates from chicken, CIPARS *Retail Meat Surveillance*, 2003–2012



The Maritimes area is sampled as a region (New Brunswick, Nova Scotia, Prince Edward Island). Due to unforeseen and protracted lengthy delays in retail sampling in the Maritimes in 2012, in the interest of precision, the data are incomplete and not presented for this year. Data for this region will be presented again in 2013.

Resistance among *Campylobacter* from retail chicken was relatively low in 2012 (<16%) with the exception of tetracycline resistance. Ciprofloxacin resistance continued to decline in British Columbia in 2012 (8%) compared to 2011 (13%), and remained at a similar level in Saskatchewan (5%) compared to 2011 (4%). In Ontario, ciprofloxacin resistance significantly increased in 2012 (16%) compared to 2003 (4%). More details are available in the case study by Agunos et al., in this issue (4). Resistance to azithromycin (Category II) was significantly lower in 2012 (8%) than in 2003 (22%) in Québec (**Figure 2**).

FIGURE 2. Temporal variation in resistance to selected antimicrobials in *Campylobacter* isolates from chicken, CIPARS Retail Meat Surveillance, 2003–2012



The Maritimes area is sampled as a region (New Brunswick, Nova Scotia, Prince Edward Island). Although routine retail surveillance began in the Maritime region in 2008, no results are displayed for that year due to concerns regarding harmonization of laboratory methods.

Due to unforeseen and protracted lengthy delays in retail sampling in the Maritimes in 2012, in the interest of precision, the data are incomplete and not presented for this year. Data for this region will be presented again in 2013.

No ciprofloxacin resistance was observed in retail chicken *E. coli* isolates in 2012. Overall, resistance to Category I β-lactams remained similar to those in 2011. In Saskatchewan, resistance to ceftiofur was significantly higher in 2012 (22%) than in 2005 (4%), and in Québec, resistance to ceftiofur was also significantly higher in 2012 (25%) than in 2006 (6%).

Pork and beef

As in previous years, resistance to Category I β-lactams remained low (≤1%) in beef *E. coli* isolates in 2012. No ciprofloxacin resistance was observed in 2012. Similarly, among generic *E. coli* isolates from pork, resistance levels of the Category I β-lactams, including ceftiofur, remained at comparable levels to previous years in each region.

Discussion

In Canada, as is the case worldwide (5), there is evidence of resistance to medically important antimicrobials among bacteria from retail meats. Resistance among organisms isolated from poultry, beef and pork at retail is characterized by wide variation over time and across different regions. A key strength of the CIPARS system is that data from its various components (e.g., farm, clinical animal, abattoir, retail, human) can be analyzed, compared and integrated together to better understand the epidemiology of

antimicrobial resistance in food-borne bacteria in Canada. Two notable and relatively recently identified integrated issues are described below.

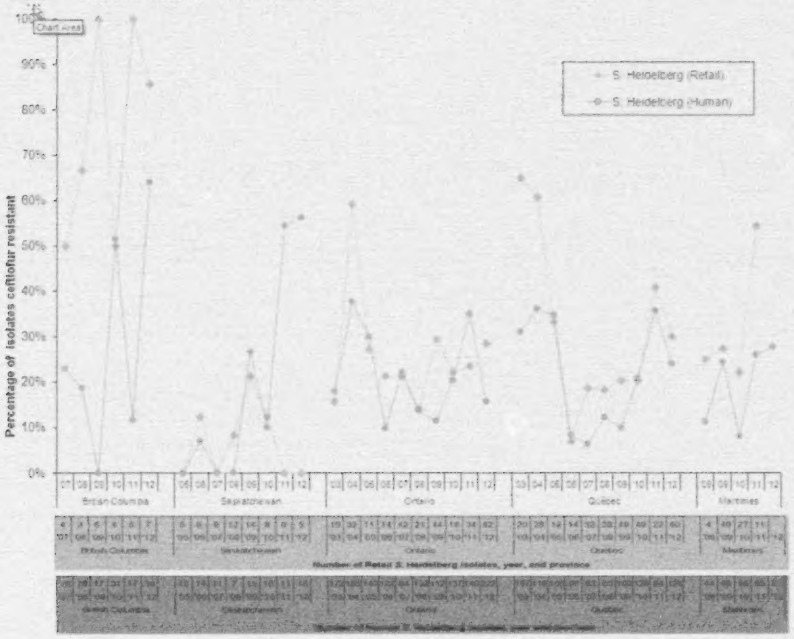
Ceftiofur resistance in *Salmonella* Heidelberg

Ceftiofur is used to treat and prevent a wide variety of infectious animal diseases. Although it is not labelled for use in chickens in Canada, it has been used to control *E. coli* omphlitis (yolk sack infection) in broiler chicks. Due to the mechanism of resistance, if a bacterium is resistant to ceftiofur, it is almost always resistant to ceftriaxone and all other third generation cephalosporins. Ceftriaxone is one of the drugs of choice for treating severe salmonellosis and other food-borne bacterial infections in pregnant women and children.

Changes in the level of ceftiofur resistance in *S.* Heidelberg were observed between 2003 and 2008 (6). More recent data from 2011 and 2012 show that, regardless of the source of *S.* Heidelberg (human or retail meat), resistance to Category I β-lactams (specifically ceftiofur and ceftriaxone) remained relatively high (**Figure 3**). Across Canada, 27% of human *S.* Heidelberg isolates were resistant to both ceftiofur and ceftriaxone in 2012. Although *S.* Heidelberg was less frequently recovered from people in Western Canada, the proportion of isolates resistant to ceftiofur and ceftriaxone was higher: 51% of *S.* Heidelberg isolates from people in the four western provinces demonstrated resistance, whereas 21% of isolates from the eastern provinces of Canada were resistant.

As in previous years, resistance to ceftiofur and ceftriaxone was also commonly observed in *S.* Heidelberg isolates from agri-food sources in 2012. Among *S.* Heidelberg isolates from retail chicken meat, 32% (30/94) were resistant to ceftiofur and ceftriaxone; by region, resistance ranged from 0% in Saskatchewan to 86% in British Columbia (**Figure 3**). As in people, *S.* Heidelberg was more commonly observed in chicken meat from Eastern Canada. Although much less common in Western Canada, a higher percentage of the isolates demonstrate resistance to Category I β-lactams.

FIGURE 3. Temporal (2003–2012) variation in ceftiofur resistance in *Salmonella* Heidelberg isolates from retail chicken and humans

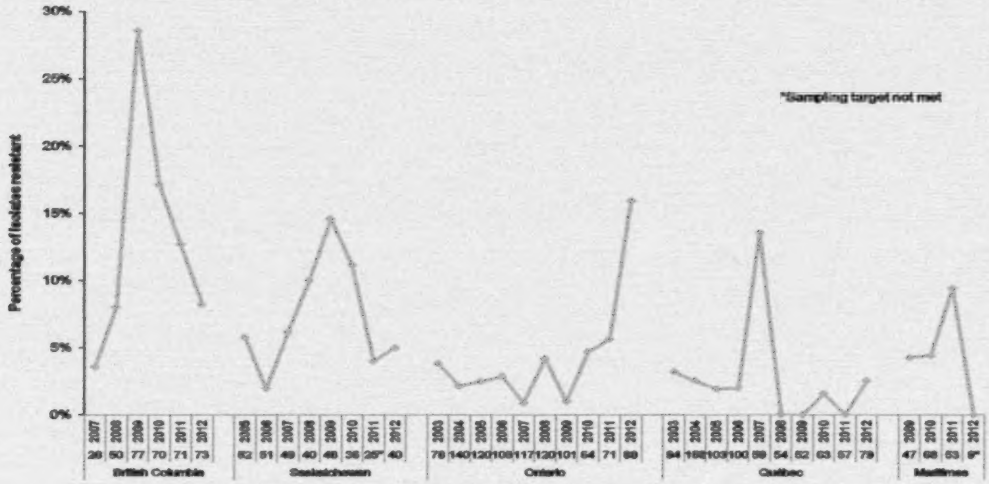


Ciprofloxacin resistance in *Campylobacter*

Over the past several years, ciprofloxacin resistance has been observed in *Campylobacter* isolates, particularly those from retail chicken (7,8). As noted earlier, important and changing regional differences in the level of resistance were observed in 2012 (**Figure 4**). In British Columbia, the proportion of ciprofloxacin-resistant *Campylobacter* continued to decline in 2012 (8%), down from a high of 29% in 2009. In 2012, Ontario had the highest proportion (16%) of ciprofloxacin-resistant *Campylobacter* from retail chicken in that year; this is the highest level of ciprofloxacin resistance observed to date in the province. More information about this important health issue and how it is influencing surveillance and policy decisions in Canada is presented by Agunos et al., in this issue (4).

Ciprofloxacin resistance in *Campylobacter* was also observed in isolates recovered from samples collected at slaughter in 2012. Ciprofloxacin resistance was observed in 6% (8/152) of isolates from cattle, 7% (11/155) of chicken isolates, and 10% (28/287) of pig isolates. It is important to note that abattoir isolates are recovered from samples of cecal contents and meant to be more reflective of the bacterial population on the farm rather than contamination at the slaughter plant. Slightly higher level of resistance in isolates from pigs may be attributed to the species of *Campylobacter* recovered (*C. coli* is the most common species in pigs; *C. jejuni,* is the most common species in chicken).

FIGURE 4. Temporal variation in resistance to ciprofloxacin in *Campylobacter* isolates from chicken; CIPARS Retail Meat Surveillance, 2003–2012



Year, number of isolates tested (chicken), number of isolates tested (turkey), and province/region

Conclusion

Antimicrobial resistance will continue to challenge the health of Canadians and of people around the world for some time to come. CIPARS data is used to detect changes in resistance over time and across Canada, and to help inform the development of evidence-based policies on antimicrobial use in hospital, community, and agricultural settings. Ongoing collection of surveillance data will help document the effectiveness of these changes to prolong the effectiveness of antimicrobial drugs.

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The authors would like to acknowledge the effort of the CIPARS retail field workers, sampling node coordinators, and laboratory technicians for their contributions. We would also like to thank the participating health units and environmental health officers/public health inspectors for sampling in remote areas in British Columbia and Ontario, and the provincial public health laboratories for their support of the human component of CIPARS. Lastly, the authors would like to acknowledge the University of Prince Edward Island for retail sampling and laboratory support in the Maritime provinces. The careful collection of samples, processing of isolates, and recording of results are essential to the ongoing success of CIPARS.

Conflict of interest

None.

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Ciprofloxacin-resistant *Campylobacter* in broiler chicken in Canada

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Abstract

This case study outlines the patterns of ciprofloxacin resistance in *Campylobacter* isolated from retail chicken meat in Canada. *Campylobacter* is the third most common cause of foodborne enteric illness in Canada; it usually causes a self-limited illness, but in some cases antimicrobials may be indicated. Ciprofloxacin (a fluoroquinolone) is an antimicrobial used to treat a number of infections in humans; other fluoroquinolones are used both therapeutically and prophylactically in livestock animals, including broiler chickens. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) has been testing retail chicken meat samples across Canada for the presence of *Campylobacter* and for resistant strains since 2003. At the end of 2010, CIPARS documented that retail chicken meat samples in Canada contaminated with *Campylobacter* ranged from 36% in the Maritimes to 42% in British Columbia. Furthermore, levels of ciprofloxacin-resistant *Campylobacter* varied across the country, with higher percentages in British Columbia (17% in 2010) and Saskatchewan (11%), in comparison with lower percentages in Ontario (5%), Québec (2%, and the Maritimes (4%). In 2011 and 2012, resistance declined in British Columbia and Saskatchewan, but began to rise in Québec and Ontario. Recently, the Canadian poultry industry developed a policy to eliminate the preventive use of third generation cephalosporins and fluoroquinolones in broiler chickens (meat chickens) and broiler breeder chickens (chickens that produce the eggs that will become the broilers). CIPARS will continue to monitor trends in antimicrobial use and resistance following this industry intervention. By following good food preparation and hygiene practices, Canadians can reduce the risks of developing a *Campylobacter* infection (resistant or susceptible) from retail chicken.

Introduction

Antimicrobials have been commonly used in treating a multitude of infectious diseases and health challenges present in both humans and animals. This case study outlines the patterns of ciprofloxacin resistance in *Campylobacter* isolated from retail chicken meat in Canada, explores its potential implication to human health and identifies what is being done to address it. It is a story of how Canada's "farm-to-fork" surveillance system, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), detected this resistance pattern and tracked it as it emerged across the country. We also identify the impact of this information on the use of antimicrobial drugs in the Canadian poultry industry and what further steps are being taken to better understand and decrease this potential threat to both human and animal health.

Campylobacter

Recent estimates showed that approximately 90% of an estimated 1.6 million cases of domestically acquired foodborne illnesses in Canada are caused by four pathogens: *Norovirus, Clostridium perfringens, Campylobacter*, and non-typhoidal *Salmonella* (1, 2). The majority of *Campylobacter* infections are usually self-limiting, causing diarrhea, abdominal cramping, fever, headache, and myalgia.

Campylobacter infections are thought to be acquired mainly through consumption of contaminated food products, with a smaller proportion of cases caused by direct contact with farm animals, pets, and

contaminated recreational waters. Case control studies have identified a significant association between human campylobacteriosis and consumption of raw or undercooked poultry (3).

Treatment with antimicrobials is generally not required for uncomplicated cases, but may be necessary for treating vulnerable patients or those with severe, prolonged or systemic infections. In the event treatment is needed, the macrolide drugs erythromycin or azithromycin are recommended, with ciprofloxacin as an alternative drug (4). However, in a study of antimicrobial use and resistance in two health units in Ontario, 45 of the 138 human cases of campylobacteriosis used ciprofloxacin (5).

Ciprofloxacin

Ciprofloxacin is a fluoroquinolone antimicrobial commonly used in humans for the treatment of respiratory, urinary, skin, and bone/joint infections, as well as some cases of gastroenteritis in adults (6). Fluoroquinolones are considered "critically" or "very" important to human medicine (Category I) by the World Health Organization (7) and Health Canada's Veterinary Drugs Directorate (8).

Fluoroquinolones are used only for rare or sporadic bacterial disease outbreaks in chickens or in treating severe infections where commonly used antimicrobials proved ineffective (i.e., an increasing number of sick and/or dead birds noted in the flock despite antimicrobial use) (9). In Canada, enrofloxacin is licensed only for use in cattle, pigs, dogs, and cats, and danofloxacin is licensed only for cattle. These fluoroquinolone antimicrobials are not approved for use in poultry. According to Health Canada's Veterinary Drugs Directorate, this class of antimicrobial should not be used for mass medication purposes (i.e., to treat an entire flock or herd of animals) in an extra-label manner (i.e., in a manner that is not in accordance with the label or package insert) (10).

Antimicrobial resistance surveillance

The Public Health Agency of Canada coordinates CIPARS, a surveillance system that monitors antimicrobial use in humans and animals as well as antimicrobial resistance (AMR) in select bacteria from humans, animals and food (11). The agri-food component of this Program consists of surveillance through sentinel farms providing herd- or flock-level data on antimicrobial use and AMR; abattoir (slaughter plant) surveillance, providing national representative AMR data for bacteria isolated from animals as they enter the food supply; and retail surveillance, providing data on AMR for bacteria found in raw meat purchased at grocery stores reflecting consumer exposure to antimicrobial resistant bacteria in food. Quantities of antimicrobials distributed for sale for use in animals in Canada are also provided to CIPARS by the Canadian Animal Health Institute. Bacteria of interest are *Salmonella*, generic *Escherichia coli*, and *Campylobacter*.

Detection of ciprofloxacin-resistant *Campylobacter* in retail chicken samples

CIPARS has been testing retail chicken samples across Canada for the presence of *Campylobacter* since 2003, starting with Ontario and Québec and in additional provinces in more recent years. By the end of 2010, the percentage of retail chicken samples found to be contaminated with *Campylobacter* ranged from 21% in Québec to 42% in British Columbia (12).

Between 2005 and 2010, CIPARS observed an increase in the prevalence of ciprofloxacin resistance among the *Campylobacter* recovered from retail chicken meat. In particular, significant differences in the provincial prevalence of resistance were identified; resistance was observed to be rising in British Columbia (4% in 2007 to 17% in 2010) and Saskatchewan (6% in 2005 to 11% in 2010), while remaining relatively low and stable among retail chicken isolates collected in Ontario (4 % in 2003 to 5% in 2010), Québec (3% in 2003 to 2% in 2010), and the Maritimes (0 % in 2008 to 4% in 2010 (12).

Several communication strategies were used to notify public and veterinary health stakeholders of these findings. In the summer of 2010, the Ministries of Health and Agriculture in British Columbia and

Saskatchewan were notified and poultry veterinarians were consulted. In the summer of 2011, this issue was raised through a CIPARS Surveillance Bulletin (13) to inform the Canadian poultry industry, other commodity and veterinary organizations, and public health stakeholders. In the summer of 2013, a meeting was organized with poultry industry stakeholders to provide an update on these findings. During the CIPARS national multi-commodity stakeholder meeting in the fall of 2013, this issue was further highlighted and more recent data presented.

CIPARS continues to monitor this issue through the farm, abattoir, and retail surveillance components and continues to see changes in the levels of ciprofloxacin resistance across the country. In 2012, both British Columbia and Saskatchewan showed decreasing levels of ciprofloxacin resistance in *Campylobacter* from retail chicken since the original notifications, with prevalences of 8% and 5%, respectively. However, in 2012, increased resistance was found in areas where resistance had previously been rare. In Ontario, for example, resistance increased from 6% in 2011 to 16% in 2012, while in Québec resistance increased from 0% in 2011 to 3% in 2012 (14). This observation was confirmed by CIPARS abattoir surveillance data where a similar trend in ciprofloxacin resistance was noted among chicken *Campylobacter* isolates.

Assessment and public health action

Ciprofloxacin-resistant *Campylobacter* from retail chicken in Canada has become more widespread over the last few years (2011 and 2012) (14), although the extent and the trends vary according to region. The drivers of the emergence of resistant *Campylobacter* in retail chicken samples are unknown at this time, but the extra-label use of fluoroquinolones in broilers, broiler breeders, and imported hatching eggs and chicks have been hypothesized as a contributing factor (12).

Other factors may be at play here however. The literature suggests that on-farm sources and operational factors could contribute to the spread of antimicrobial resistant *Campylobacter*. A systematic review of the literature suggests that antimicrobial resistant *Campylobacter* may be disseminated within a flock through the drinking water line and could spread across the farm through farm workers (via contaminated footwear) (15). *Campylobacter* has been reported to be spread by chicken catching crews that travel from farm to farm and then onto slaughter plants when birds were exposed to contaminated poultry equipment at transport (15). The slaughter of chickens from *Campylobacter*-positive farms was associated with the contamination of chicken meat products (11, 13, 14).

Implications to human health

Human *Campylobacter* infections have been linked to the consumption of contaminated poultry meat products (16–19). A study conducted in the United States has shown that ciprofloxacin-resistant *Campylobacter* infection can result in prolonged infections (19). More recently, a Canadian study found that human *Campylobacter* isolates are often genetically related to chicken isolates (20), but susceptibility data for human infections are limited and are currently not available for surveillance systems in Canada.

A previous U.S. risk assessment report (2000) has shown that chicken products contaminated with ciprofloxacin-resistant *Campylobacter* contribute to ciprofloxacin-resistant *Campylobacter* infections in humans (21). Consequently, good food safety and hygiene practices are more important than ever to ensure the reduction in transmission of resistant and susceptible *Campylobacter* from contaminated meat to people. This includes appropriate wrapping and placement of chicken in refrigerators, careful washing of surfaces and utensils that touch raw chicken, using different surfaces for preparing raw meat and vegetables/fruit, and thorough cooking (22).

Effect on industry policy response

Recently, the Canadian poultry industry developed a policy to eliminate the preventive use of antimicrobials considered of very high importance to human medicine; these include third generation cephalosporin and fluoroquinolone antimicrobials (23). This policy took effect in May 2014 for broilers and will take effect in May 2015 for broiler breeders and turkeys (23). A one-year extension of the implementation of this policy will allow the industry to inform key stakeholders of this change.

Effect on surveillance

In April 2013, CIPARS initiated surveillance of antimicrobial use and antimicrobial resistance at the broiler farm level. This new surveillance component will help investigate the relationships between antimicrobial use and resistance and will track the potential impact of recent industry policy changes on the occurrence of resistance in *Campylobacter* and other enteric pathogens from poultry.

Discussion and conclusion

CIPARS documented that ciprofloxacin-resistant *Campylobacter* in retail chicken occurs across the country; levels in Western Canada have been dropping, but the previously low to absent levels in Eastern Canada have been rising.

Antimicrobial resistance risk management has no quick fix; patterns of antimicrobial use can take a long time to change and patterns of resistance can also take a long time to disappear. Despite the progress that has been made, CIPARS continues to detect ciprofloxacin-resistant *Campylobacter* in retail chicken in Canada. It is still unclear how resistance to fluoroquinolones emerged in *Campylobacter* from broilers in Canada, and if and how it spread from the Western to Central and Eastern regions, or if it emerged independently.

The driver of fluoroquinolone use in this sector also remains unclear. The Veterinary Drugs Directorate established a policy recommending against the extra-label use of Category I antimicrobial drugs in food-producing animals (10); however, this lies under the purview of practice of veterinary medicine to enforce. Initial data from the farm program suggest that limited extra-label use of fluoroquinolones is occurring in Canadian broiler chicken flocks. CIPARS will continue to monitor farm drug usage and reasons for use (i.e., prophylactic or therapeutic) and to evaluate associations between antimicrobial use and resistance.

CIPARS previously identified gaps in the surveillance of *Campylobacter* and antimicrobial use practices in Canada. As a result, surveillance of antimicrobial use and resistance at the broiler farm level in Canada was initiated in April 2013; these new data are being used to investigate the relationships between antimicrobial use and resistance as well as the impact of recent policy changes. In addition, CIPARS is currently determining the best approach to carry out AMR testing of human *Campylobacter* infections to better understand the public health impact of exposure to ciprofloxacin-resistant *Campylobacter* through retail chicken meat and other sources.

CIPARS will continue to monitor trends in antimicrobial use and resistance following industry's intervention eliminating the preventive use of Category I antimicrobials (of very high importance to human medicine). However, by following good food preparation and hygiene practices, Canadians can reduce the risks of developing a *Campylobacter* infection from retail chicken.

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New resources to address antibiotic resistance are just a click away

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Abstract

Antibiotic resistance is a complex issue with multiple causes, and there are many roles to play in addressing it. As part of its response, the Public Health Agency of Canada is launching a pilot antibiotic awareness campaign for Canadian families and health care professionals. Coinciding with Antibiotic Awareness Week, starting on November 17, 2014, the goal of this campaign is to improve knowledge and awareness of antibiotic resistance in Canada. To achieve this, the Agency has developed a suite of resources for both Canadian families and health care providers featuring a variety of key messages explaining antibiotic resistance, why it is important, and how to reduce the risks associated with it. Resources for Canadian families include an online informational video, an educational brochure, and infographics for both adults and children. Resources for health care professionals include two online Continuing Medical Education Modules, a letter that physicians can sign and provide to parents explaining why an antibiotic was not prescribed, and two webinars to present trends in antimicrobial resistance (AMR) and antimicrobial use. Health professionals will also receive an electronic postcard and a bilingual campaign poster. Promoting the campaign messages and using these campaign resources will support health professionals in discussions about antibiotic resistance with their patients or clients, and in their continuing efforts to be part of the solution in addressing this important global health challenge.

Introduction

Antibiotic resistance is a growing health concern around the world that threatens our ability to effectively treat many illnesses and infections (1). This is a complex issue with multiple causes, and there are many roles to play in addressing it. The Public Health Agency of Canada (the Agency) leads the Government of Canada's response to the issue of antibiotic resistance in Canada. Part of this response includes the development and launch of a pilot antibiotic awareness campaign for Canadian families and health care professionals. The launch of the Agency's pilot awareness campaign will coincide with Antibiotic Awareness Week, which takes place November 17–23, 2014. Antibiotic Awareness Week is recognized in Canada and internationally. The purpose of this article is to brief health care professionals about the Agency's campaign and associated resources.

Goal, key messages and resources

The objective of this campaign is to improve knowledge and awareness of antibiotic resistance in Canada through the promotion of responsible antibiotic use and good infection prevention behaviours. To support this goal, the Agency will be promoting several key health promotion messages to Canadians that explain what antibiotic resistance is, why it is important, and how to reduce the risks associated with it. Key messages include:

- Antibiotic resistance is a public health concern.
- Sometimes no prescription is the right prescription.

- There are easy steps that can be taken to reduce the risk of getting an antibiotic resistant infection.
- Always use antibiotics as directed.

To achieve its objective, the Agency has developed a suite of resources to address antibiotic resistance, intended for both Canadian families and health care providers (2). Resources for Canadian families include: an online informational video; an educational brochure—*Antibiotic Resistance: Questions & Answers*; two infographics for adults—*Antibiotic Resistance: Facts and Figures*, and *Help Reduce Antibiotic Resistance*; as well as an infographic for children aged 8–12 entitled *Germs & Antibiotics*.

Resources for health care professionals include two online Continuing Medical Education Modules: one on antimicrobial resistance (AMR) in general, and another specifically on AMR and gonorrhea. As they become available, these modules can be accessed on the Government of Canada's Shared Services e-learning website as well as on the websites of various health professional associations. Resources will also include, for example, a letter that physicians can sign and provide to parents explaining why an antibiotic was not prescribed for their child; this is designed to further assist with the education of the general public on this important public health issue. In addition, two webinars are planned for November 2014 to launch the campaign and to present findings from the Agency's surveillance programs on Canadian trends in antimicrobial resistance and antimicrobial use (see index page).

In the coming weeks, health professionals will receive an electronic postcard from Dr. Howard Njoo, Director General of the Agency's Centre for Communicable Diseases and Infection Control, with links to these campaign resources on antibiotic resistance. Canadian family physicians, general practitioners, and pediatricians, will also receive bilingual print copies of the campaign poster and of the education brochure that can be used to help inform patients; Canadian pharmacies will receive print copies of the education brochure.

Conclusion

Canada has already seen positive changes in prescribing practices aimed at curbing antimicrobial resistance (3). To further support your efforts, the Agency encourages you to visit the Government of Canada antibiotic resistance website to learn more about antibiotic use and resistance in Canada and to access our resources (2). Promoting the campaign messages and using these campaign resources will support your discussions about antibiotic resistance with your patients or clients, and in continuing your efforts to be part of the solution in addressing this global health challenge.

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